

UNIT 17

ETHERS |

Structure

17.1	Introduction	Physical Properties
	Expected Learning Outcomes	Reactions of Open Chain Ethers
17.2	Classification	Reactions of Epoxides
17.3	Preparation of Ethers	17.5 Crown Ethers and Cryptands
	Preparation of Open Chain Ethers	17.6 Industrial Uses
	Preparation of Epoxides	17.7 Summary
17.4	Properties of Ethers	17.8 Terminal Questions
		17.9 Answers

17.1 INTRODUCTION

In the previous Unit 15, while discussing the chemistry of alcohols, it was pointed out that mono alkyl derivatives of water are called alcohols and dialkyl derivatives of water are called ethers. In this unit, we will study the chemistry of ethers in detail.

In this unit, we first discuss the structure and classification of ethers. Then, we will study the preparations, physical properties and chemical properties of both open chain ethers and a group of cyclic ethers, called epoxides. We shall also touch on a special group of macrocyclic (large ring) compounds, called crown ethers and cryptands.

Expected Learning Outcomes

After studying this unit, you should be able to:

- ❖ list different types of ethers such as open chain ethers, epoxides, crown ethers and cryptands;
- ❖ outline the preparation of open chain ethers and epoxides;
- ❖ explain the physical properties of ethers;
- ❖ describe the chemical properties of open chain ethers and epoxides;

The Nobel Prize for Chemistry in 1987 was given to Charles J. Pedersen, Donald J. Cram and Jean-Marie Lehn, for their efforts in discovering and determining uses of crown ethers and cryptands, thus launching the new growing field of Supramolecular Chemistry.

- ❖ describe the crown ethers and cryptands; and
- ❖ state the industrial uses of ethers and related compounds.

17.2 CLASSIFICATION

Like water and alcohols, ether molecule contains an sp^3 hybridised oxygen atom, which is bonded to two carbon atoms. Fig. 17.1 shows the structure of dimethyl ether $[\text{CH}_3\text{OCH}_3]$ also with its ball-stick model. In this molecule, two sp^3 hybrid orbitals of oxygen form two σ bonds with the two carbon atoms. Similar to water molecule the other two sp^3 hybrid orbitals of oxygen each contain an unshared pair of electrons. The C–O–C bond angle in dimethyl ether is 110.3° , a value close to the tetrahedral angle of 109.5° .

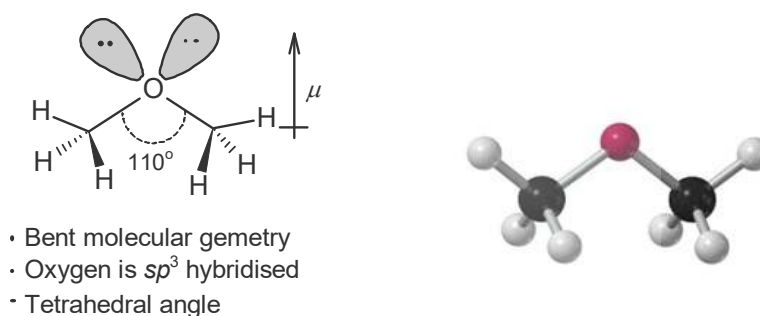
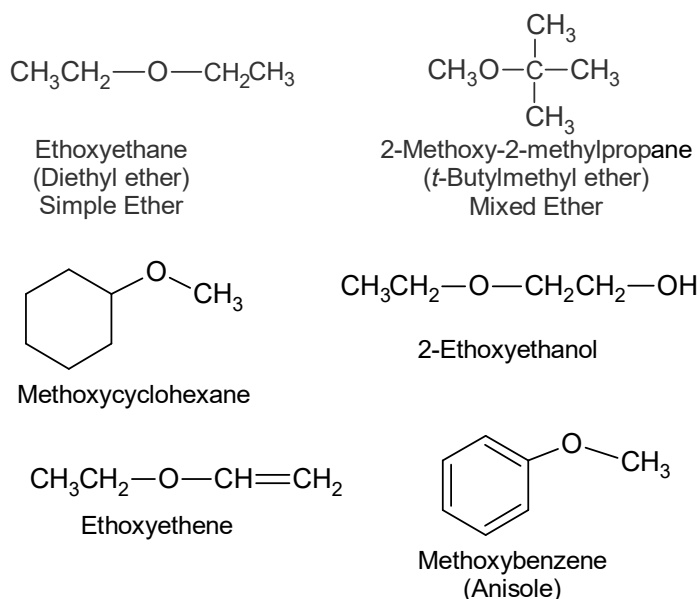
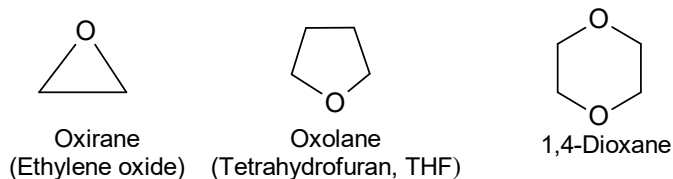


Fig. 17.1: Structure of dimethyl ether along with its Ball-and-Stick model. Here μ represents net dipole moment in the molecule.

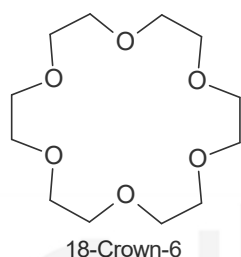
The groups bonded to the ether oxygen can be alkyl, aryl, ethenyl or any other carbon containing group. Aliphatic ethers may be simple or symmetrical in which both the alkyl groups are the same or mixed i.e. unsymmetrical in which the two alkyl groups are different. Just to recall, in IUPAC system of nomenclature, ethers are named by selecting the longer carbon chain as the parent alkane and namely the $-\text{OR}$ group bonded to it as an alkoxy group. Common names are derived by listing the alkyl group bonded to oxygen in alphabetical order and adding the word ether. Now consider few examples of simple ethers (name given in brackets are common names):



Ethers can be either open chain or cyclic. When the ring size (including the oxygen atom) is five or greater, the chemistry of the cyclic ether is similar to that of an open chain ethers. Three membered cyclic ethers are called oxiranes (IUPAC name), which are often known as epoxides. Because of Baeyer strain associated with small rings, epoxides are more reactive than other ethers.

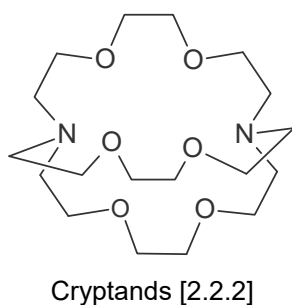


Large ring system with repeating $-\text{OCH}_2\text{CH}_2-$ units are called crown ethers. They are macro-monocyclic polyethers. These compounds are valuable reagents which can be used to help dissolve inorganic salts in organic solvents. Crown ethers are named as x-crown-y; where x is the total number of atoms in the ring and y is the total number of oxygen atom in the ring. For example,

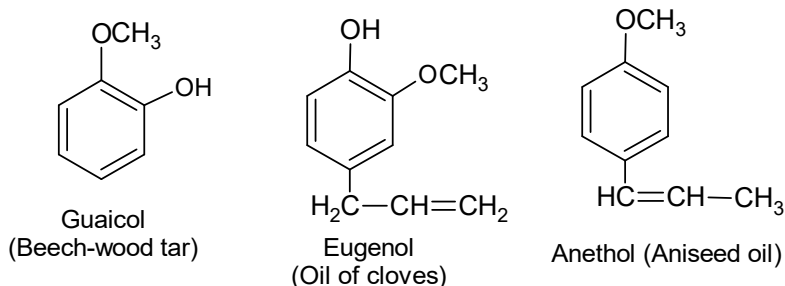


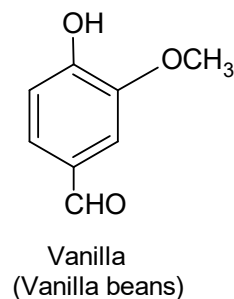
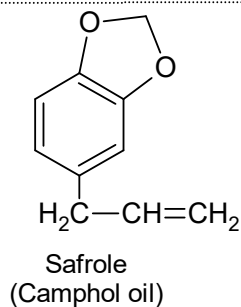
A crown ether with a total number of 18 atoms and 6 oxygen atoms in the ring

There is another class of compounds, similar to crown ethers, called cryptands. These are macro-polycyclic polymers having additional bridge(s). These compounds show higher complexing ability and selectivity towards a variety of metal ions in comparison with crown ethers. In the example of cryptand [2.2.2] given below, the numbers in the brackets indicate the numbers of ether oxygen atoms in the chains between the bridgehead nitrogen atoms.



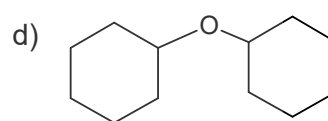
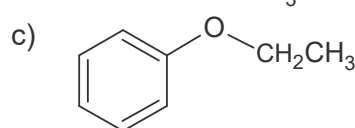
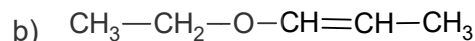
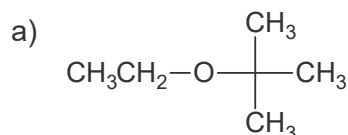
Ethers occur widely in nature, some examples of naturally occurring ethers are:





SAQ 1

Write IUPAC and common names for the following ethers:



17.3 PREPARATION OF ETHERS

In this section, we will discuss the preparation of open chain ethers and epoxides.

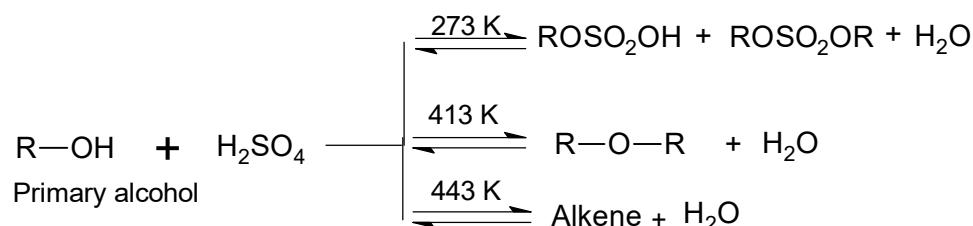
17.3.1 Preparation of Open Chain Ethers

Ethers are commonly prepared from alcohols. There are two methods:

- Acid catalysed dehydration
- Nucleophilic displacement (Williamson ether synthesis)

i) Acid Catalysed Dehydration

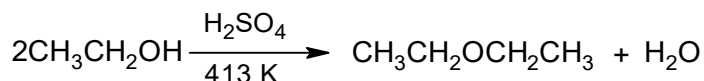
In precious Unit 15, we have described the conversion of alcohols to alkenes in the presence of sulphuric acid. When an alcohol is reacted with H_2SO_4 , a series of reversible reactions occur under different reaction conditions. Which reaction product predominates depends on the structure of the alcohol, the relative concentration of reactants, and temperature of the reaction mixture.



As shown above, primary alcohols give alkyl hydrogen sulphate and dialkylsulphate at low temperatures, symmetrical ethers at moderate temperature and alkenes at high temperature.

In case of secondary alcohols, yields of ethers are lower because of competition from acid-catalysed dehydration. In case of tertiary alcohols, dehydration to an alkene is the only reaction.

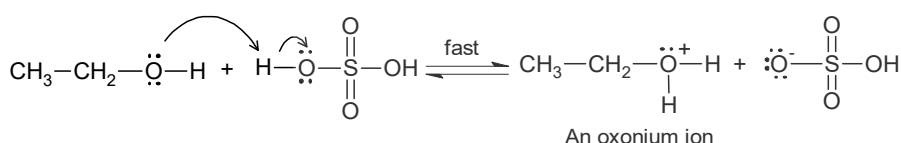
Diethyl ether is synthesised on an industrial scale by the acid-catalysed dehydration of ethanol.



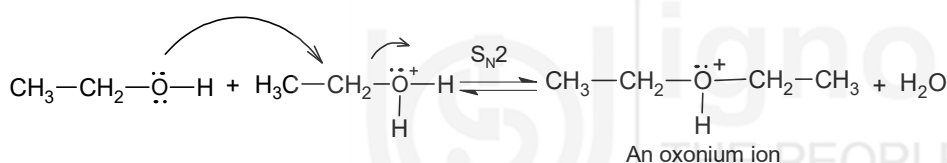
Reaction Mechanism: Acid-catalysed dehydration of ethanol:

It follows the $\text{S}_{\text{N}}2$ mechanism. Detailed steps are as follows:

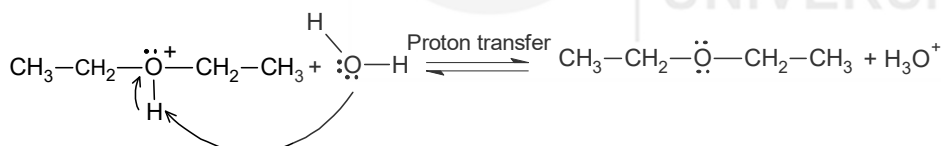
Step 1: Acid converts $-\text{OH}$, a poor leaving group into $-\text{OH}_2^+$ a better leaving group



Step 2: The protonated ethanol is attacked by another molecule of ethanol (nucleophile) in an $\text{S}_{\text{N}}2$ process, thus, displacing H_2O .



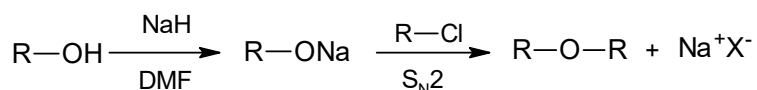
Step 3: Deprotonation



Notice that a proton is used in the first step of the mechanism and then another proton is liberated in the last step of the mechanism. Therefore, in this reaction, the acids behave as a catalyst.

ii) Williamson Ether Synthesis

Ethers are also prepared by Williamson ether synthesis. This method is the most common general method for the preparation of ethers. This process is named after Alexander Williamson, a British scientist who first demonstrated this method in 1850 as a method of preparing diethyl ether. This method involves nucleophilic displacement of halide ion or other good leaving group by an alkoxide ion ($\text{S}_{\text{N}}2$ mechanism). If alcohols are starting material, one alcohol preferable primary alcohol is converted to alkyl halide (R-X), another alcohol is converted to alkoxide, using strong base such as sodium hydride (NaH), and then, the two products are heated together.

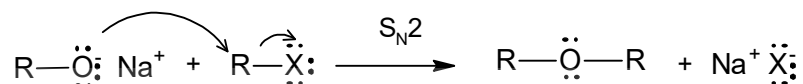


Mechanism: Williamson Ether Synthesis: This is a two step reaction.

Step 1: Hydride ion function as a base and deprotonates the alcohol.



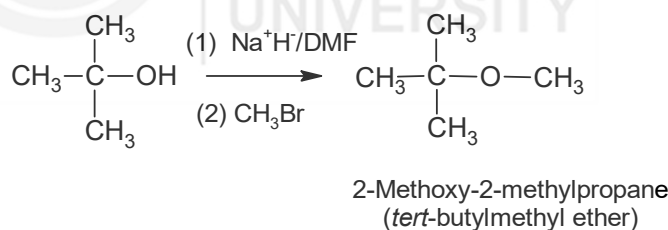
Step 2: The resulting alkoxide ion then functions as nucleophile and attacks the electrophilic carbon centre of alkyl halide and displacing halide ion.



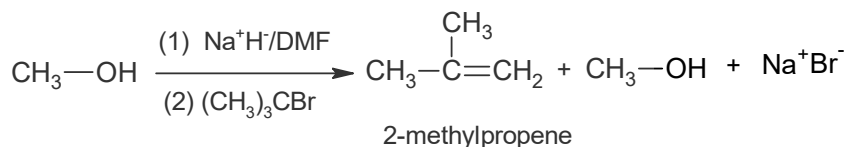
As mentioned earlier, because of steric effect, the tendency for alkyl halide to undergo $\text{S}_{\text{N}}2$ reaction is $\text{primary} > \text{sec} > \text{tert}$. Therefore, this process works best with methyl or primary alkyl halides. Secondary alkyl halides are less efficient because elimination is favoured over substitution and tertiary alkyl cannot be used. This limitation must be kept in mind while designing a synthesis of ethers. For example consider the synthesis of *tert*-butylmethyl ether which is also known as methyl-*tert*-butyl ether (MTBE). There can be two possible routes, one by the reaction of butyl alcohol and bromomethane or other by the reaction of methanol with 2-bromo-2-methylpropane (*tert*-butyl bromide). The first route is efficient because it takes place through a primary alkyl halide i.e. bromomethane; which is suitable for $\text{S}_{\text{N}}2$ reaction. On the other hand; the second route does not work because it employs a tertiary alkyl halide which will undergo elimination reaction ($\text{E}2$) rather than substitution.

MTBE was used to improve octane rating of gasoline until it was observed the MTBE might contribute to ground water contamination.

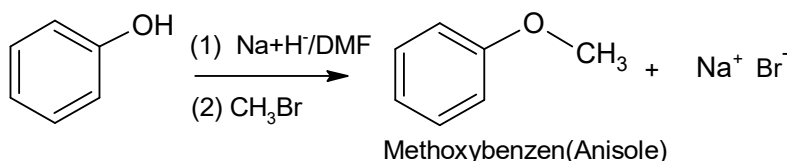
Route 1:



Route 2:

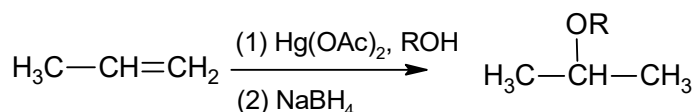


This method can also be used to prepare phenolic ethers.

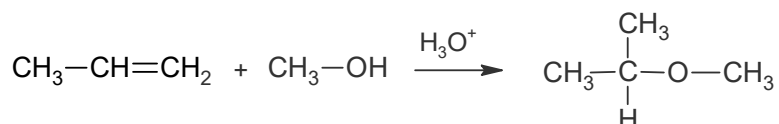


If you wish to prepare methoxybenzene by the reaction of methanol and chlorobenzene in presence of strong base; this reaction does not work. Because the chlorine atom in chlorobenzene is attached to sp^2 carbon and $\text{S}_{\text{N}}2$ process does not occur at sp^2 -hybridised centre.

Ethers can also be prepared by the reaction of alcohols with alkenes. Recall the oxymercuration-demercuration reaction of alkenes. If alcohol is used in place of water, the final product is ether which is result of the addition of alcohol across the alkene. This addition reaction follows Markovnikov mechanism.



Similar to above reaction, alcohol can also be added to alkenes in the presence of acid to give ethers.



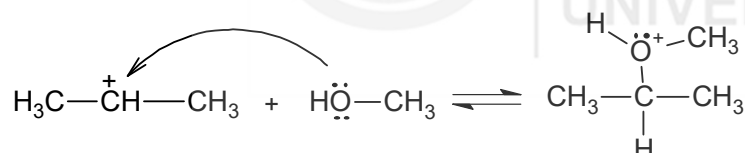
Mechanism: Acid catalyzed addition of an alcohol to an alkene.

This reaction follows $\text{S}_{\text{N}}1$ mechanism.

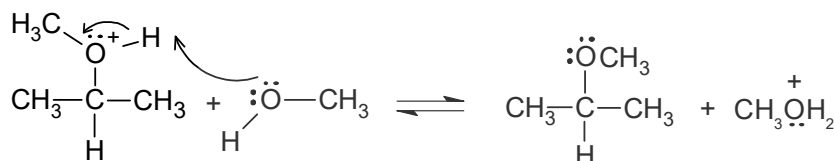
Step 1: Proton transfer from the acid to the alkene gives a carbocation intermediate.



Step 2: Reaction of the carbocation intermediate (an electrophile) with the alcohol (a nucleophile) gives an oxonium ion.



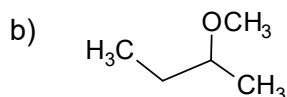
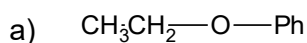
Step 3: Proton transfer to solvent



This method is used for the industrial production of MTBE. This method is only suitable for the reactions of alkenes which can produce stable carbocations with methanol or primary alcohols.

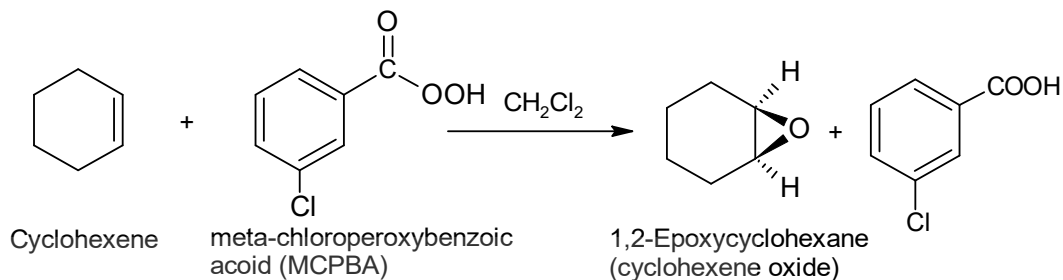
SAQ 2

Show the reagents that can best be used to prepare following ethers by Williamson ether synthesis:

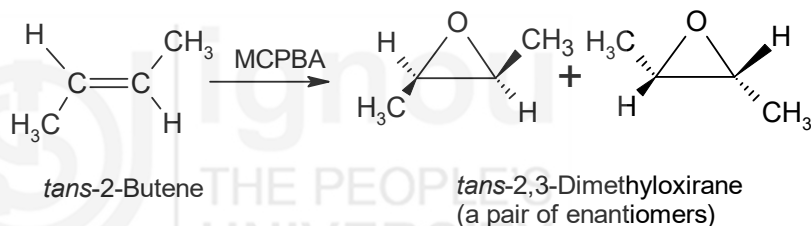
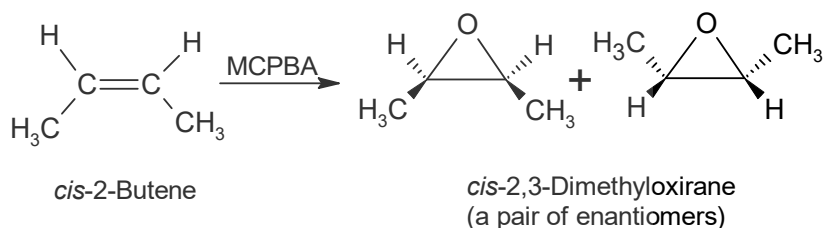


17.3.2 Preparation of Epoxides

Epoxides are obtained by the reaction of alkenes with peracids. This is most common method for synthesis of epoxides. Among per acids *meta*-chloroperoxybenzoic acid (MCPBA) is the most commonly used per acid.

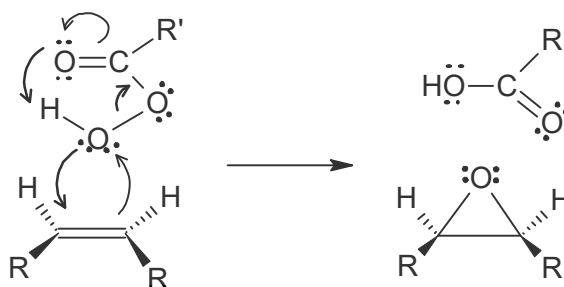


This reaction is stereo specific (not entioselective); that is, the *cis* alkene give *cis* epoxides and *trans* alkene give *trans* epoxides.

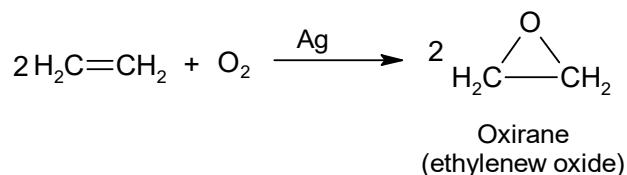


Mechanism: Epoxidation of an alkene by peracids.

In this reaction, bond-making and bond-breaking steps are taking place simultaneously i.e. in concerted way.

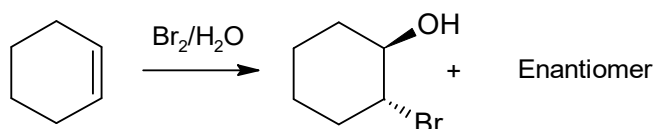


Industrial preparation of oxirane (ethylene oxide) is carried out by passing a mixture of ethylene and air (or oxygen) over a silver catalyst.

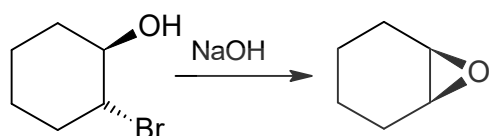


This method only works for the production of oxirane from ethylene. There are other methods also by which, we can prepare epoxides. In the previous Unit

15, we have seen that alkenes can be converted to halohydrins when they are treated with halogens in presence of water.



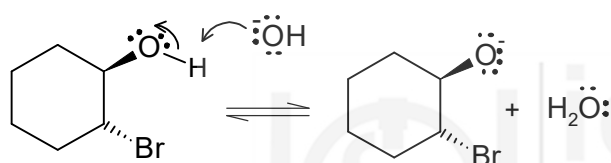
The halohydrin obtained from above reaction can be converted into epoxides upon treatment with a strong base.



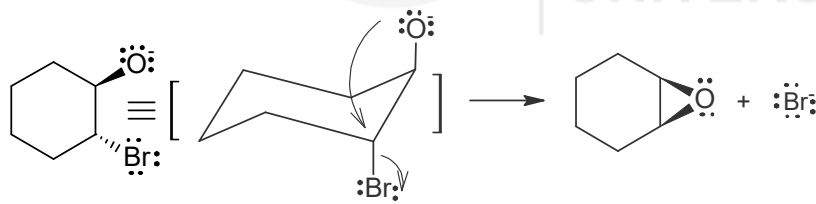
This reaction follows intra molecular $\text{S}_{\text{N}}2$ mechanism.

Mechanism: Epoxide formation from halohydrin.

Step 1: Hydroxide ion or other base abstract a proton from the hydroxyl group of halohydrin to form an alkoxide ion.

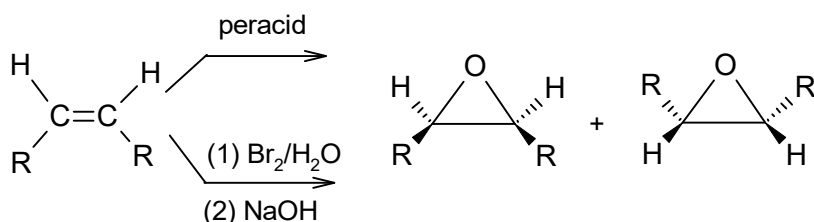


Step 2: Alkoxide ion formed in Step 1, functions as a nucleophile in an intramolecular $\text{S}_{\text{N}}2$ reaction, removing the halide as a leaving group.

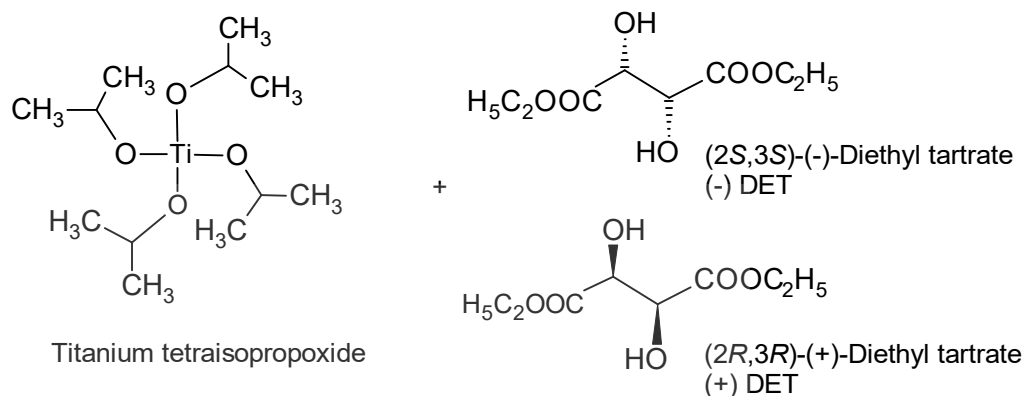


As with all $\text{S}_{\text{N}}2$ reactions, attack of the nucleophile is from the back side of the C-X bond and causing inversion of configuration at the site of substitution.

The stereochemical outcome of this conversion is the same as the reaction of peracids with alkene. That is, substituents that are *cis* to each other in the starting alkene remain *cis* to each other in the epoxide; and similarly substituents that are *trans* to each other in the starting alkene remain *trans* to each other in the epoxide.



Both the conversion routes provide a racemic mixture. In recent past, Prof. Barry Sharpless developed a catalyst for the **asymmetric (stereoselective) epoxidation of allylic alcohols**. The Sharpless' catalyst consists of titanium tetrakisopropoxide $[\text{Ti}(\text{O-iPr})_4]$, and pure enantiomer of diethyl tartrate [(+) or (-) DET].



In the presence of any one of the above chiral catalyst, an oxidising agent such as *tert*-butylhydroperoxide converts an allylic alcohol to enantioselective epoxide. The stereochemical outcome of the reaction depends on whether the chiral catalyst used was (+) DET or (-) DET.

In Fig.17.2, we have shown that how oxygen is delivered to either the top face or the bottom face of the alkene, depending on which enantiomer of diethyl tartrate is used.

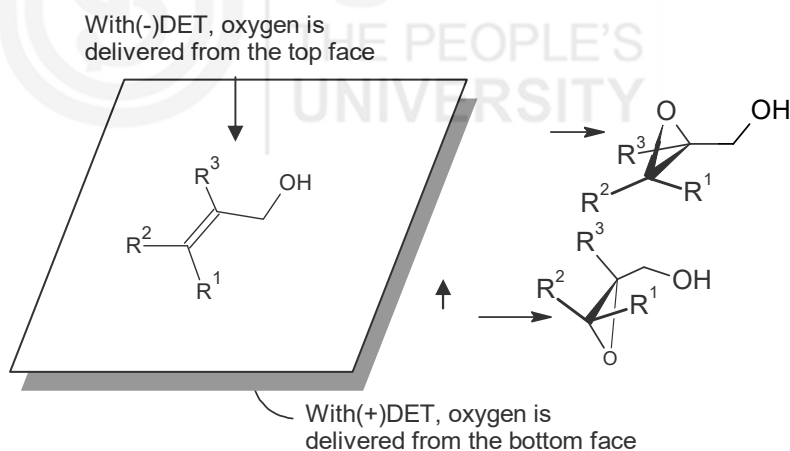
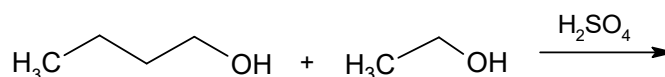


Fig. 17.1: Sharpless asymmetric Epoxidation.

Sharpless along with William Knowles and Ryoji Noyori received the 2001 Noble Prize in Chemistry for their pioneering work in the field of asymmetric synthesis.

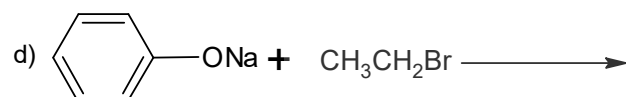
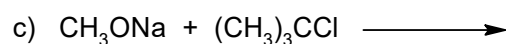
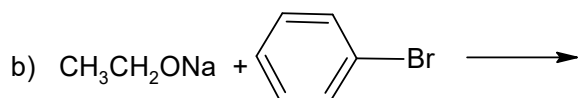
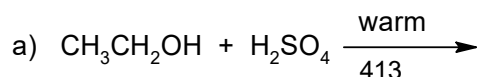
SAQ 3

Explain why the following reaction is not preferred for the preparation of ether.



SAQ 4

Predict the major product of these reactions:



17.4 PROPERTIES OF ETHERS

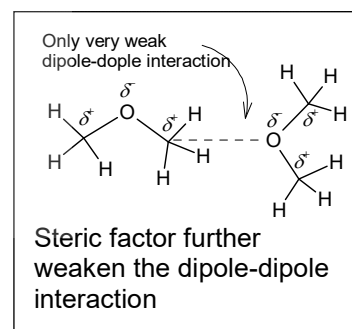
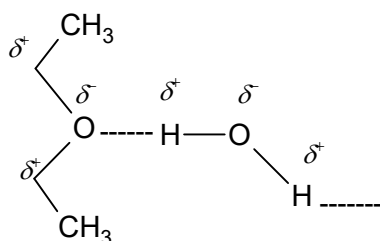
Before studying the reactions of open chain ethers and epoxides in detail, let us first understand their physical properties.

17.4.1 Physical Properties

As discussed earlier, the geometry of the oxygen atom in ethers is similar to water and alcohols. Oxygen atom is sp^3 hybridised and the orbitals are arranged in a tetrahedral shape. Thus, similar to water and alcohols, due to the high electronegativity of oxygen atom, ethers are polar compounds with dipole moment $3.9 \times 10^{-30} \text{ C m}$ for diethyl ether. But they are not as polar as water, $6.0 \times 10^{-30} \text{ C m}$ and alcohols, $5.7 \times 10^{-30} \text{ C m}$ (for methanol). Because of the weak dipole – dipole interactions, ethers have lower boiling points as compared to those of alcohols containing the same number of carbon atoms and are close to those of hydrocarbons of having comparable carbon numbers. Another factor which also influences the boiling points of compounds is intermolecular hydrogen bonding, which is present in case of alcohols and not feasible in case of ethers because they do not have hydrogen attached to the oxygen and thus they cannot function as hydrogen bond donors.



	$\text{CH}_3\text{CH}_2\text{OH}$	$\text{CH}_3\text{—O—CH}_3$	$\text{CH}_3\text{CH}_2\text{CH}_3$
Boiling point	Ethanol 352 K	Dimethyl ether 249 K	Propane 273 K

As ethers cannot act as hydrogen bond donors they are much less soluble in water than alcohols. However, they can act as hydrogen bond acceptors, which make them more soluble in water than hydrocarbons.



We are summarizing the physical properties of some of ethers in Table 17.1. For the comparison, boiling points of some alcohols are also given.

Table 17.1: Physical properties of some ethers

Name	Formula	Bp, K	Solubility in H ₂ O	Density kg/dm ³
Diethyl ether	CH ₃ OCH ₃	249	Miscible	Gas
Ethanol	CH ₃ CH ₂ OH	351	(Highly soluble)	0.79
Diethyl ether	C ₂ H ₅ OC ₂ H ₅	307.6	8 g/100 cm ³	0.71
1-Butanol	CH ₃ (CH ₂) ₂ CH ₂ OH	380	8.3 g/100 cm ³	0.81
Methyl phenyl ether (anisole)	C ₆ H ₅ -O-CH ₃	427		
Tetra hydro furan (THF)		339	Miscible	0.89
Oxirane		286.5	Miscible	8.88 (at 283 K)

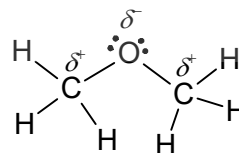
Before studying the reactions of ethers, try following SAQ.

SAQ 5

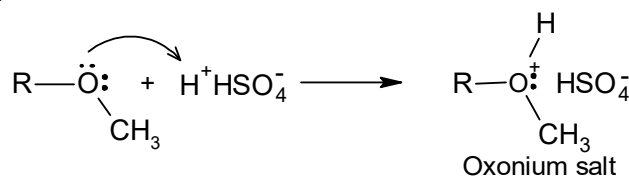
To what effect can you attribute for water solubility of ethers?

17.4.2 Reactions of Open Chain Ethers

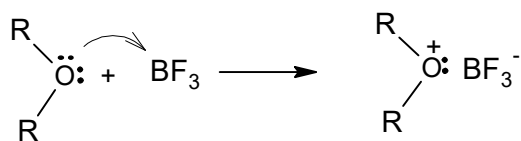
Ethers are quite unreactive and behave more like alkanes than like organic compounds containing functional groups. As a result, they are ideal choice as solvent for many reactions. The bond between carbon and oxygen in ether is called the ether linkage. This ether linkage is not affected by even strong bases, oxidising agents such as potassium dichromate or potassium permanganate. However, due to the presence of highly electronegative oxygen atom in ether, the carbon atoms bonded to oxygen behave as electrophilic centres at which nucleophilic reaction can occur.



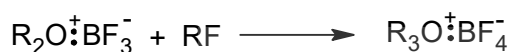
Further due to the presence of lone pair on oxygen, ethers behave as Lewis bases (electron-pair donors). Therefore, with strong acids, ethers give oxonium salts:



The solubility of ethers in sulphuric acid is, thus, a convenient method for distinguishing between ethers and hydrocarbons and alkyl halides. Similarly, ethers react with Lewis acid to form Lewis complexes.



Further, this Lewis complex treatment with alkyl fluoride gives a tertiary oxonium salt, trialkyloxoniumtetrafluoroborate.

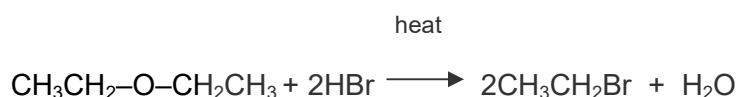


The product of above reaction i.e. the, trialkyloxoniumtetrafluoroborates are powerful alkylating agents in many reactions.

As shown above, ethers have two electrophilic centres. Therefore, ethers may undergo **nucleophilic substitutive reaction**. But in the case of ethers, nucleophilic substitution reaction can only be possible with a reagent that can react first with the oxygen atom of ether to form a good leaving group and then also provide a good nucleophile to displace it. The strong acids such as HBr and HI fulfill these criteria. In such reactions, cleavage of the ether linkage (C – O) takes place. These reactions are called acidic cleavage reaction of ethers.

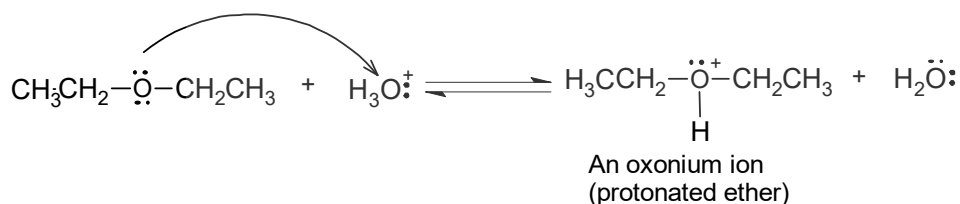
1. Acidic Cleavage

Ethers are cleared using hot, aqueous hydrobromic acid (48%) or hydroiodic acid (57%). For example diethyl ether reacts with hot concentrated HBr to give two molecules of bromoethane.

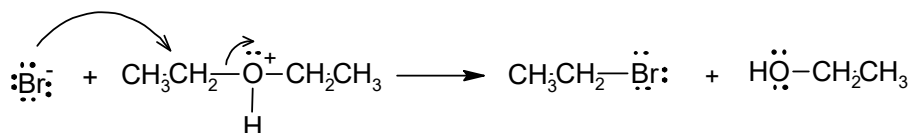


Mechanism: Acid cleavage of ethers:

Step 1: Protonation of ether molecule leads to formation of a good leaving group.



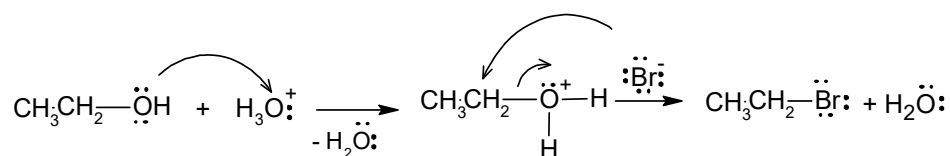
Step 2: Nucleophilic substitution reaction ($\text{S}_{\text{N}}2$): A bromide ion (Br^-) functions as a nucleophile and attacks at electrophilic centre of oxonium ion by displacing an alcohol as a leaving group.



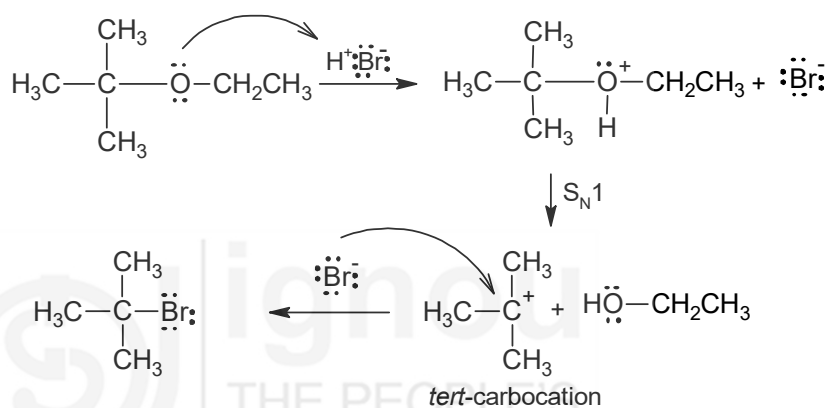
If the ether is unsymmetrical, the nucleophile prefers to attack on less hindered electrophilic carbon centre of ether. Recall the order of reactivity of $\text{S}_{\text{N}}2$ reactions:

$\text{CH}_3 > \text{primary} > \text{Sec} > \text{tert}$

This cleavage produces one molecule of bromoethane and one molecule of ethanol. In presence of excess concentrated HBr, ethanol is converted into second molecule of bromoethane by another S_N2 reaction:



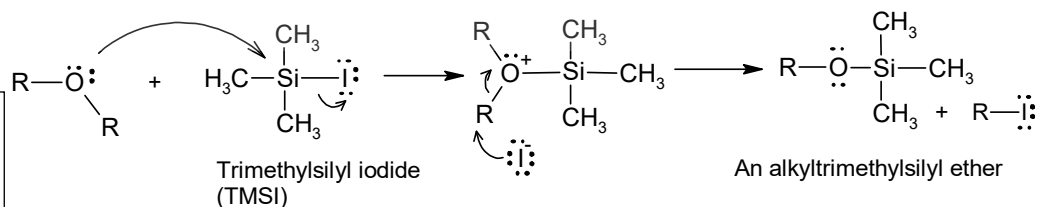
The acid cleavage of dialkyl ethers depends on the nature of the carbon bonded to oxygen. If both carbons are primary, cleavage involves an S_N2 mechanism as illustrated above. Otherwise cleavage is by an S_N1 mechanism. For example, tertiary butyl ethers, allylic and benzylic ethers follow S_N1 mechanism. These ethers require much milder reaction conditions. For example 2-ethoxy-2-methylpropane after protonation, cleaves to produce stable *tert*-carbocation.



The Zeisel procedure of estimation of the number of methoxyl (CH₃O –) or ethoxyl (C₂H₅O –) groups in alkyl and aryl ethers is based on acid cleavage reactions of ethers. This method consists of ether cleavage with excess of HI, followed by distillation of volatile iodomethane or iodoethane from the reaction mixture. Then, the iodoalkenes are treated with an ethanolic solution of silver nitrate and the silver iodide so formed is weighed.

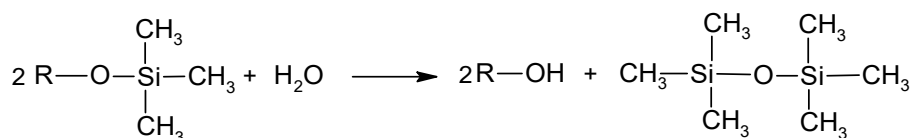
Finally, the reaction of carbocation with nucleophile completes the reaction.

Acid cleavage reactions have great importance in synthetic chemistry. The hydroxyl group in a poly functional compound can be protected by converting it into ether and later, after completion of a chemical transformation, the molecule can be regenerated after treatment with concentrate dihydroiodic acid. As HBr and HI are strong acids, therefore, we generally prefer mild reagents such as iodotrimethylsilane or trimethylsilyl iodide (TMSI)[(CH₃)₃SiI] for ether cleavage. In first step, it reacts with ether and converts ether oxygen atom to a good leaving group.

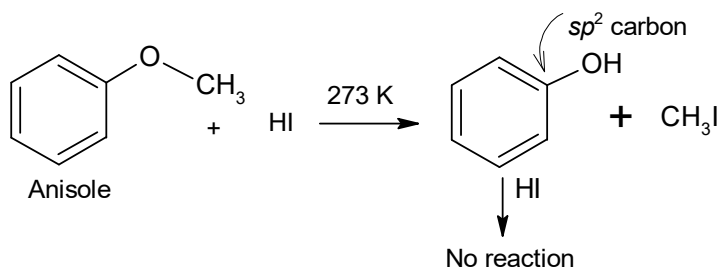


Both HI and HBr can be used to cleave ethers. HCl is less efficient and HF does not cause cleavage of ether. The reactivity is a result of the relative nucleophilicity of the halide ions.

Alcohol can be obtained by the hydrolysis of alkylmethylsilyl ether.

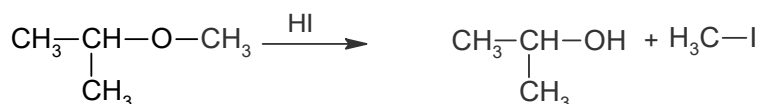


Aromatic ethers, such as anisole, yield the alkyl halide and phenol, not halobenzene and alcohol. This is because; sp^2 -hybridised carbon does not undergo reaction by an S_N2 or S_N1 path.



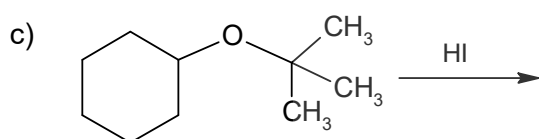
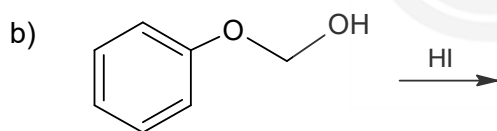
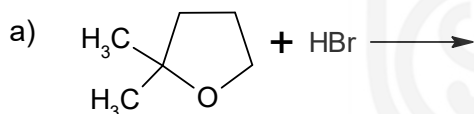
SAQ 6

Account for the fact that following reaction gives CH_3I and $(\text{CH}_3)_2\text{CHOH}$ as the initial major product rather than CH_3OH and $(\text{CH}_3)_2\text{CHOI}$.



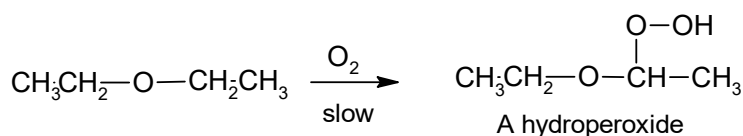
SAQ 7

Write detail mechanism pathway for the following reactions:



2. Autoxidation of Ethers

Ethers undergo autoxidation in the presence of atmospheric oxygen to form hydroperoxides:

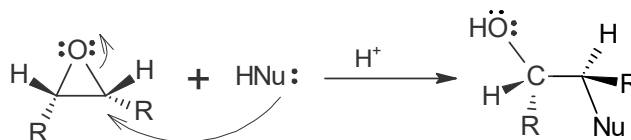


This process takes place via a free radical mechanism. The oxidised product, hydroperoxides decompose violently when heated. The presence of hydroperoxide in ether may cause laboratory explosion when ether is distilled for the purification. Therefore, it is important to know the concentration of hydroperoxide before distillation. To prevent the formation of peroxides, some

ethanol or a small amount of cuprous compound, e.g., cuprous oxide is added. It is also advised that never use ethers past their expiration date.

17.4.3 Reactions of Epoxides

It has been stated earlier that because of the strain associated with three-membered ring, epoxides are highly reactive compounds. The characteristic reaction of epoxides is nucleophilic substitution reaction. In this reaction, ring opening takes place which can be initiated either by acid (acid-catalysed ring opening) or by nucleophile (nucleophilic ring opening). The general reaction can be written as:



Characteristic reaction of epoxides

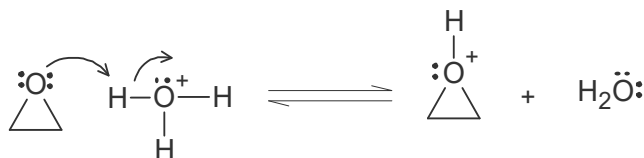
Acid-catalysed Opening

Like other ethers, epoxides undergo carbon-oxygen bond cleavage when treated with an acid. However, because of their high reactivity much milder acidic conditions are employed than for cleavage of open chain ethers. For example, acid-catalysed ring opening of oxirane gives 1, 2-ethane diol (ethylene glycol) when treated with aqueous sulphuric acid.

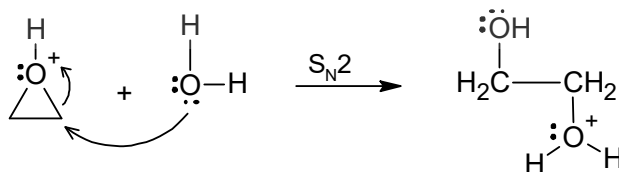


Mechanism: Acid-catalysed hydrolysis of an epoxide

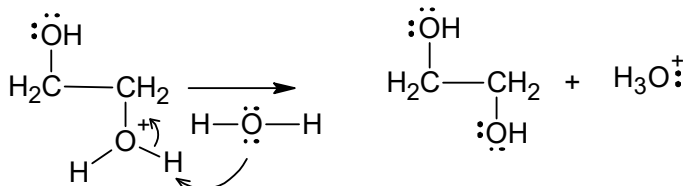
Step 1: Protonation: Proton is transferred from the acid to oxygen of the epoxide to give bridged oxonium ion intermediate



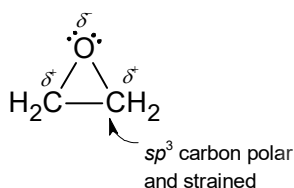
Step 2: Ring Opening: Nucleophile attacks from back side on a bridged oxonium ion and open the three membered ring.



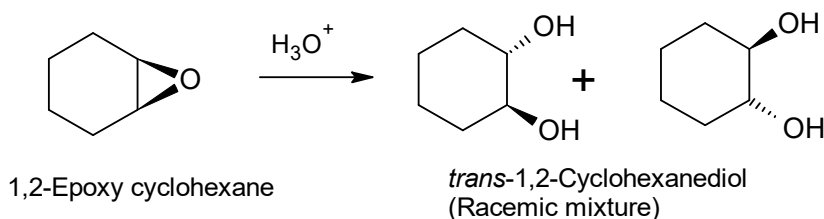
Step 3: Proton Transfer: In this final step proton is transferred to solvent.



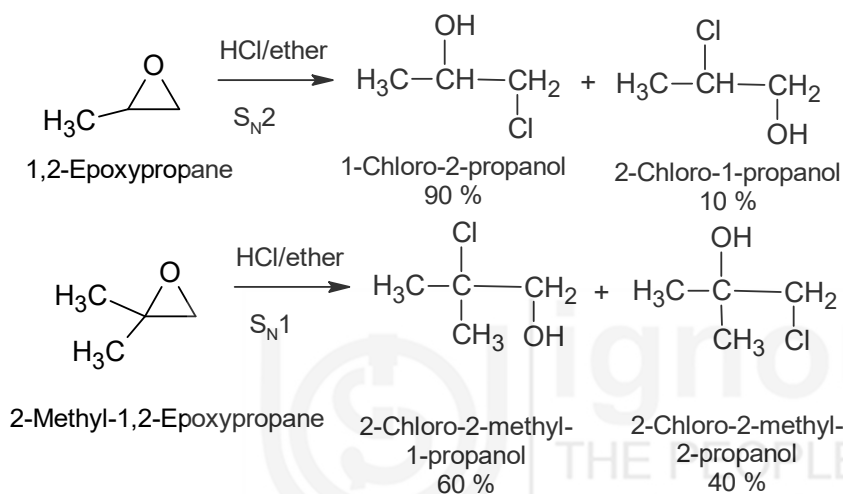
An epoxide ring cannot have normal sp^3 bond angles of 109° ; instead, the inter nuclear angles are about 60° , a geometric requirement of the three membered ring. The orbitals forming the ring bonds are incapable of maximum overlap. Therefore, epoxide ring are - strained. The polarity of the C-O bond, along with the ring strain, contributes to the high reactivity of epoxides compared to the reactivity of other ethers.



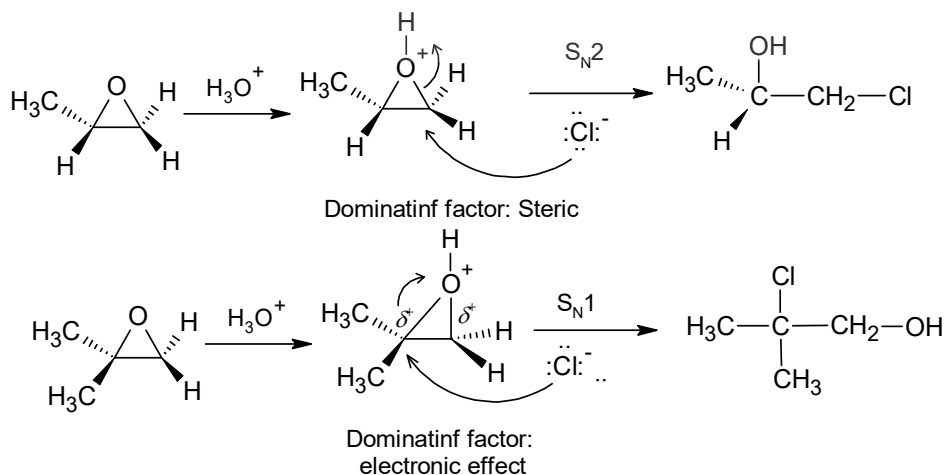
In these reactions, the attack of the nucleophile is anti to the bridge oxonium ion. Thus, the stereochemistry of acid-catalysed ring opening is S_N2 like.



But regiochemistry of these reactions depends on the nature of the epoxides. For example, if one side is primary and other side is secondary, the nucleophile will attack on the less hindered primary position following predominantly S_N2 mechanism. On the other hand, if one side of the epoxides is a tertiary the nucleophile with attack on more substituted tertiary position rather on the primary following predominantly S_N1 process.

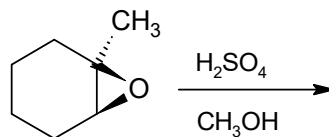


But in reality in S_N1 process, a pure carbocation does not form as we would expect for this process. Instead, an unshared electron pair on the oxygen atom maintains an interaction with the neighbouring carbon atom, which then bears only a partial positive charge. The tertiary position is significantly better at supporting a partial positive charge, so this position has significantly more partial carbocation character than the primary position or in other words more substituted carbon centre is better electrophile and therefore, more susceptible to nucleophilic attack. Because of the bridged carbocation stereochemistry of epoxides, reactions though following S_N1 process are S_N2 like. Above two acid catalysed reactions can now be illustrated as:



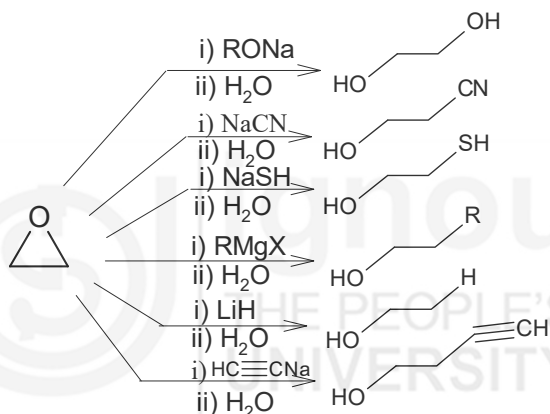
SAQ 8

Predict the product of the reaction below, and draw likely structure of oxonium ion intermediate.

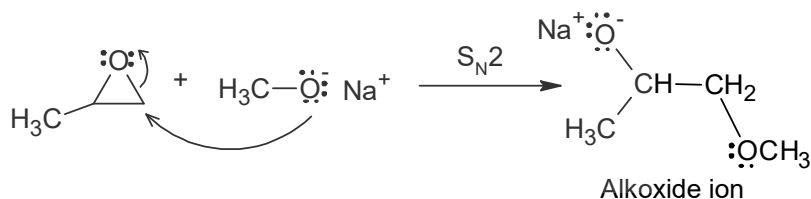


Nucleophilic Ring Opening

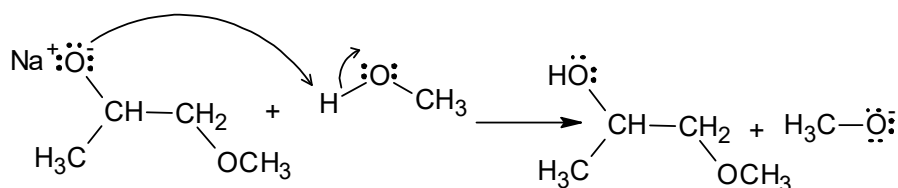
Unlike ethers, epoxides undergo ring-opening reaction with a variety of nucleophiles because of the strain associated with ring. Good nucleophiles attack on epoxides by an $\text{S}_{\text{N}}2$ mechanism and shows $\text{S}_{\text{N}}2$ like stereo selectivity and regioselectivity (inversion of configuration and nucleophile attacks the less substituted position).

**Mechanism:** Nucleophilic opening of an epoxide ring

Step 1: Nucleophile attacks from backside on the less hindered carbon of the epoxide and opens the ring by cleaving the C–O bond.

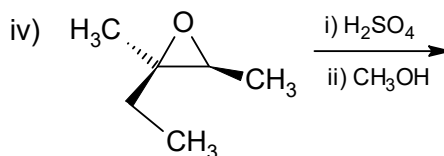
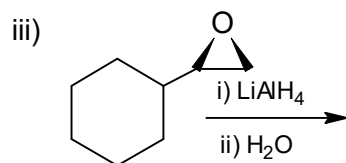
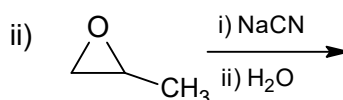
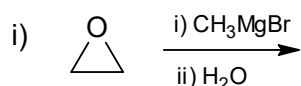


Step 2: The resulting alkoxide ion from Step 1 gets protonated by solvent system of reaction.

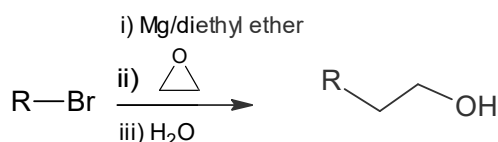


SAQ 9

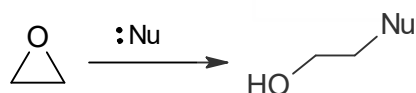
For each of the following, predict the product:



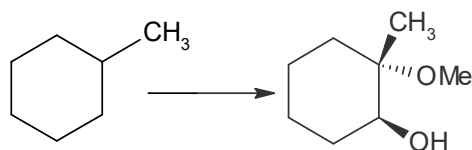
Epoxides play important role as building block in organic synthesis. Ethylene oxide can be used to introduce two carbons in a molecule. For example, consider an alkyl halide as starting material and by using an epoxide, we can introduce two carbon atoms in the structure of the alkyl halide:



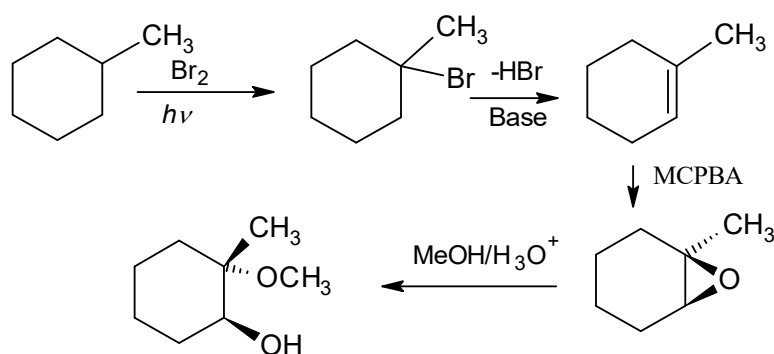
The -OH group of the product obtained from above reaction can be easily be modified by replacement with another nucleophile such as ammonia, halide, CN^- , N_3^- , SH^- etc. to get desired final or intermediate product. Epoxides can also be used for introducing functional group(s) in a molecule. You may have noticed that ring opening of an epoxide provides two functional groups on adjacent carbon centres.



For further understanding consider the following conversion:



Find product can be achieved by using following synthesis route:



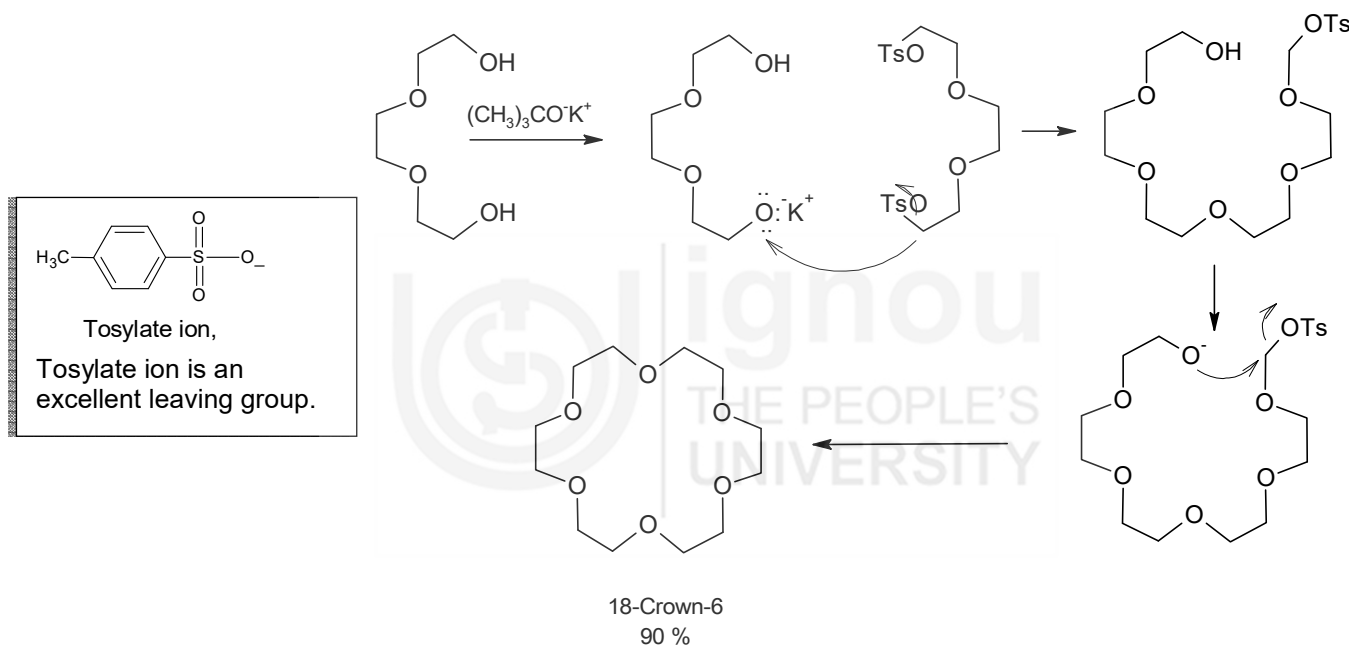
SAQ 10

How would you prepare 1-butanol from ethanol?

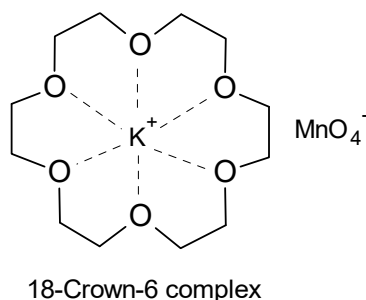
17.5 CROWN ETHERS AND CRYPTANDS

As mentioned earlier, structure of crown ethers are consisting of the repeating $-\text{OCH}_2\text{CH}_2-$ units. They are polymers of 1, 2-ethandiol. Crown ethers and cryptands have the ability to form complexes even with most reluctant alkali metal ions. This has made the coordination chemistry of alkali metals richer.

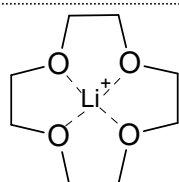
Crown ethers are prepared by a variant of the Williamson ether synthesis in which an alkoxide ion displaces a tosylate ion (It is a better leaving group than halide ions) by an $\text{S}_{\text{N}}2$ mechanism. A general procedure used for the synthesis of crown ethers is illustrated below.



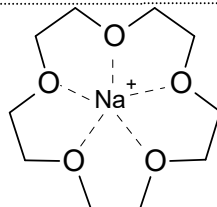
The unique feature of crown ether is that they can chelate metal ions and give metal complexes which are soluble in non-polar organic solvents. In this form, the crown ether is referred to as the host, while the metal ion is called guest. For example, purple benzene is a reagent in which KMnO_4 , complexed by 18-crown-6, is dissolved in benzene. This is a very useful reagent for the oxidation of water insoluble organic compounds.



Crown ethers are specific for the cation they bind, and this is related to the size of the cavity. As show above, 18-crown-6 binds K^+ preferentially, but smaller crown ethers can bind Li^+ or Na^+

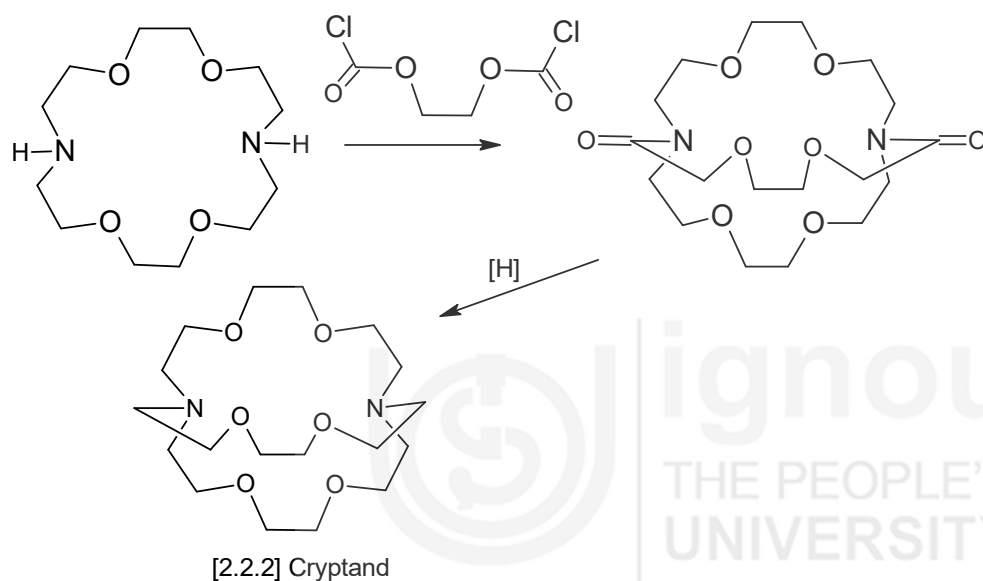


12-Crown-4



15-Crown-5

To further optimizing binding capabilities of crown ethers, Jean-Marie Lehan, who shared the 1987 Nobel Prize, developed double-cyclic crown ethers. He named them cryptands. These compounds are like crown ethers except they have addition 'bridge' which provides extra strength to hold the ion. In other words, if regular crown ether surrounds an ion, a cryptand locks it up. A typical cryptand is prepared by making a diamide from a diaza crown ether. The amide groups are subsequently reduced.



[2.2.2] Cryptand

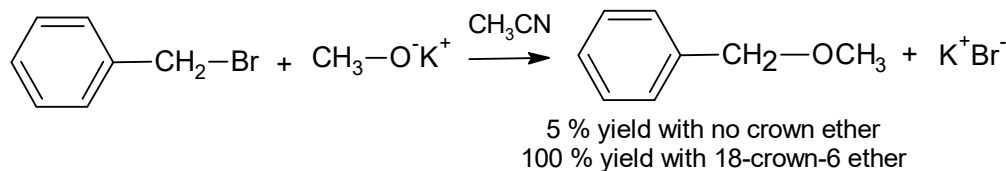
17.6 INDUSTRIAL USAGE

Ethers are widely used as solvents for oils, fats, gums, resins etc. Diethyl ether is used as refrigerant. It is also used as a solvent for extraction of organic matter, and in the laboratory for preparation of Grignard reagents. Diethyl ether was also used as inhalation anesthetic, but due to its side effects, it is now replaced by halogenated ethers such as enflurane [$\text{F}_2\text{CHOCHF}_2\text{CHClF}$], isoflurane [$(\text{F}_2\text{CHOCHClCF}_3)$], sevoflurane [$\text{CH}_2\text{FOCH}(\text{CF}_3)_2$], etc. Dimethyl ethers are used as a catalyst in industrial polymerisation process, alternative fuel, a foam expansion agent, and as an aerosol propellant for a variety of products that include adhesives, sealants, foam in a can, coating, paints, automotive care products, tropical cooling spray, hair spray, sun screen and a variety of other personal care and household products.

Because of the inert nature of the ethers, many ethers such as tetrahydrofuran (THF), 1,4-dioxane, etc. are excellent solvents for carrying out many organic reactions. Epoxides are used as intermediates in the preparation and manufacturing of other basic organic chemicals.

Crown ethers have great advantages in synthetic organic chemistry. One is that an ionic reagent can be dissolved in an organic phase where it can react

with a water-insoluble organic compound. A second advantage is that the nucleophilicity of an ion such as CN^- or CH_3COO^- is greatly enhanced in non polar solvents, where the anion is poorly solvated, or naked. An example of how a crown ether increases the rate of substitution reaction in preparation of the benzyl methyl ether in acetonitrile (methyl cyanide) which does not dissolve ionic compound is shown below.



Crown ethers generally form characteristic coloured complexes with metal ions, this property can be used for the detection of the metal ions.

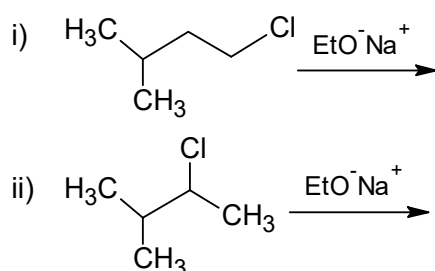
17.7 SUMMARY

What we have studied in this unit, can be summarised as follows:

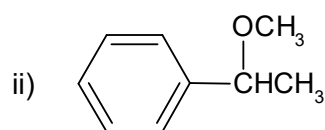
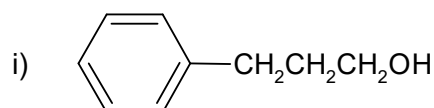
- Ethers can be prepared using the Williamson ether synthesis, which is an $\text{S}_{\text{N}}2$ reaction. On commercial scale, diethyl ether is prepared through the dehydration of ethanol in strong acid.
- Epoxides can be prepared by the reaction of peracid with alkenes or by the reaction of halohydrin with alkali.
- Ethers are less reactive than alcohols and they undergo ether cleavage by reaction with HBr and HI . This acid catalysed cleavage takes place via $\text{S}_{\text{N}}2$ or $\text{S}_{\text{N}}1$ mechanism. The exact mechanism being determined by the substituent on carbon atoms bonded to oxygen.
- Unlike ethers, epoxides are quite reactive and their ring opening reaction requires milder reaction conditions. The ring opening reaction may be initiated by acid or by nucleophile.
- The unique feature of crown ethers and cryptands is that they can selectively chelate metal ions and give complexes which are soluble in non polar solvents.
- Ethers have many industrial uses.

17.8 TERMINAL QUESTIONS

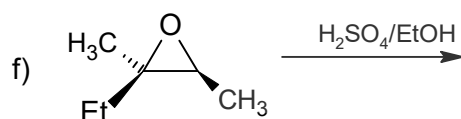
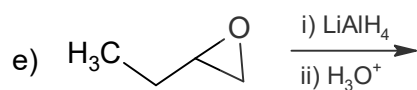
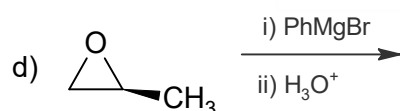
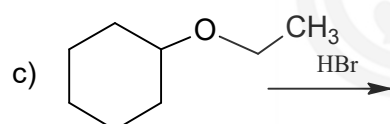
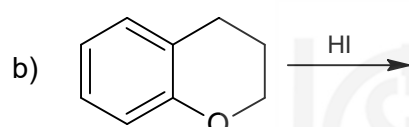
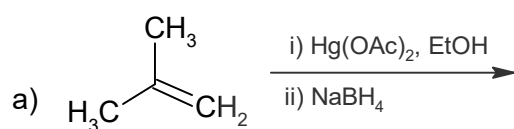
- Among ethyl alcohol and diethyl ether, which will have greater solubility in water? Explain.
- Write the major product obtained from the following reactions:



3. Write equation to show how would you prepare the following compounds?



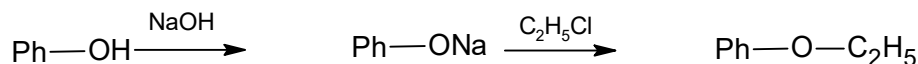
4. How are the methoxy and ethoxy groups estimated in a compound?
5. Give two important features of the crown ethers.
6. How would you prepare 1,4-dioxane from oxirane?
7. Predict the products for each of the following:



17.9 ANSWERS

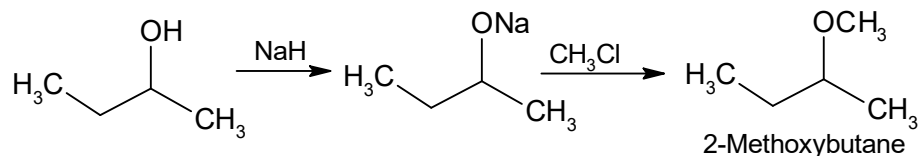
Self Assessment Questions

1. a) 2-Ethoxy-2-methyl propane; b) 1-Ethoxypropene;
c) Ethoxybenzene; d) Cyclohexyloxycyclohexane.
2. a) Following route will be followed:



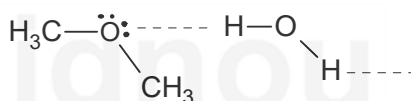
Other route using ethanol and chlorobenzene does not work as replacement of chlorine from sp^2 is very difficult.

b) Following route will be preferred:

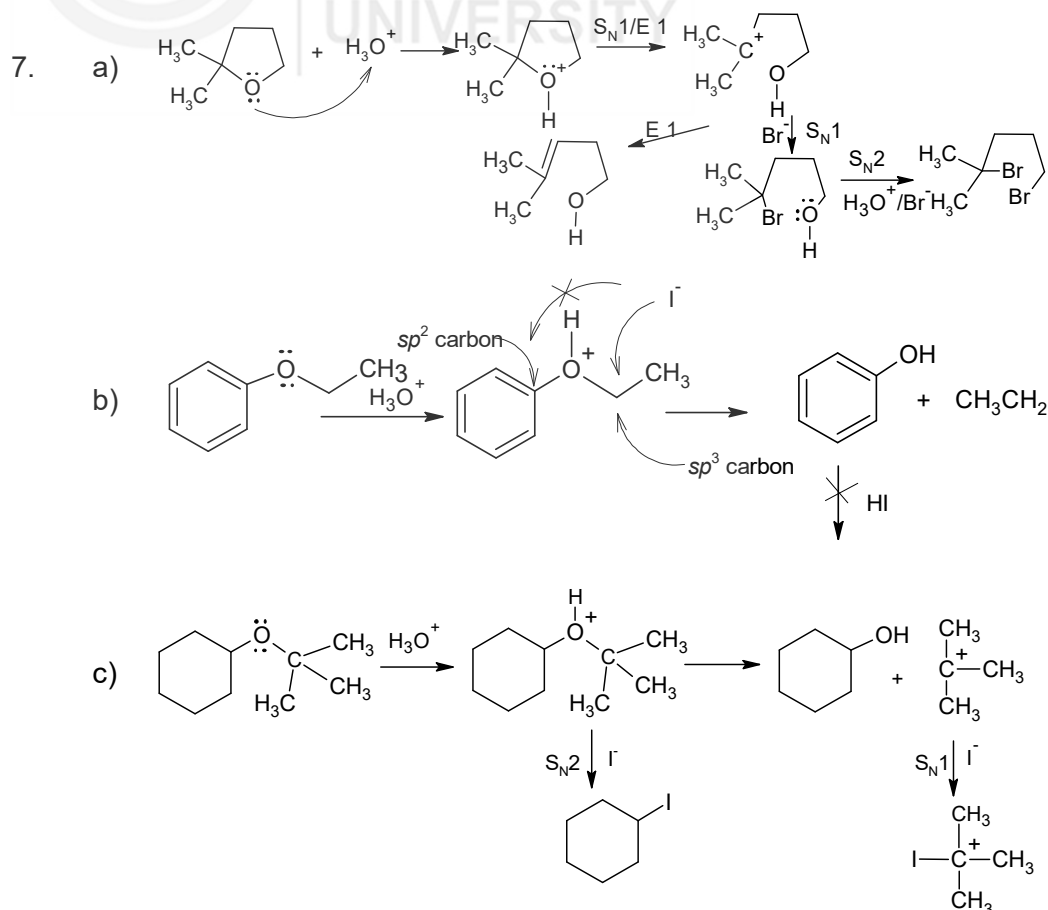


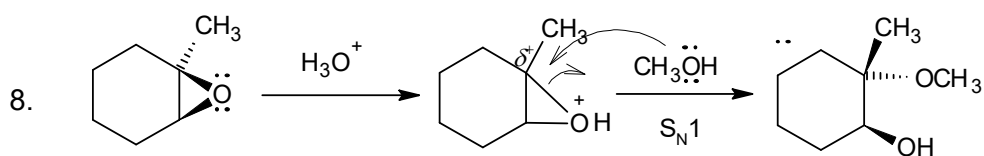
Other route using 2-chlorobutane and methanol gives considerably more elimination products.

3. From this reaction we expect a mixture of three ethers: diethyl ether, dibutyl ether and butyl ethyl ether. It is very difficult to separate these three ethers from reaction mixture in pure form.
4. a) $\text{CH}_3\text{CH}_2\text{OCH}_2\text{CH}_3$; b) No reaction, c) $\text{CH}_3\text{C}(\text{CH}_3)=\text{CH}_2$ CH_3 ; d) $\text{PhOCH}_2\text{CH}_3$.
5. Water solubility of ether can be attributed to hydrogen bonding between oxygen of ether with water.



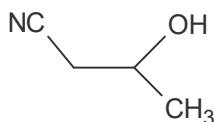
6. This reaction follows $\text{S}_{\text{N}}2$ pathway, therefore iodide ion prefers to attack on less hindered methyl carbon of 2-methoxypropane.



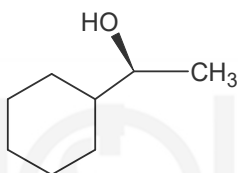


Nucleophile will attack from backside on *tert* carbon. This position is better at supporting partial positive charge. Therefore, this position has more carbocation character than *sec.* position.

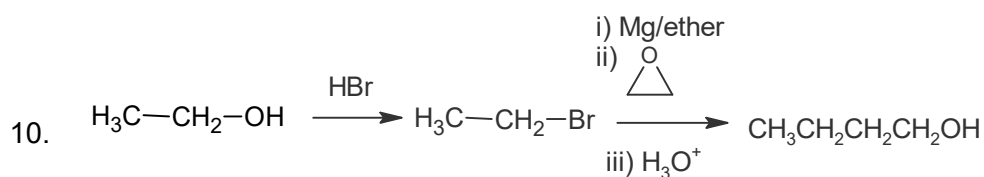
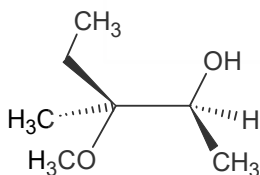
9. i) $\text{CH}_3\text{CH}_2\text{CH}_2\text{OH}$
 ii) Reaction will follow $\text{S}_{\text{N}}2$ pathway. Nucleophile will attack on less hindered position.



- iii) Reaction will follow $\text{S}_{\text{N}}2$ pathway. Nucleophile will attack on less hindered position.

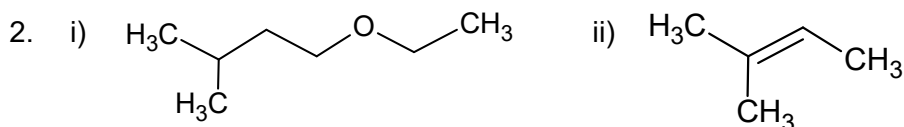


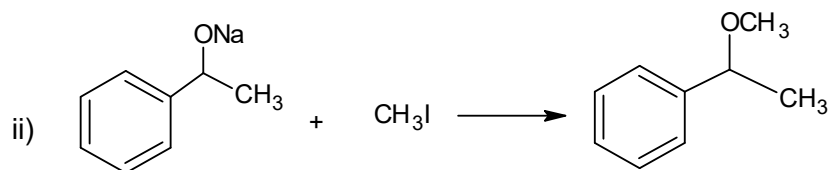
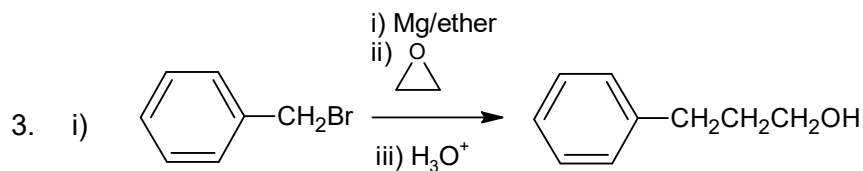
- iv) Reaction will follow $\text{S}_{\text{N}}1$ pathway. Nucleophile will attack on *tert* position.



Terminal Questions

1. Ethanol has greater solubility in water as it is more polar than ether and ethanol molecules act both as hydrogen bond donor as well as hydrogen bond acceptor. Ether is less soluble in water as its molecules cannot act as hydrogen bond donor. It only acts as hydrogen bond acceptor.





4. Methoxy or ethoxy group in an organic compound are estimated by the Zeisel method. In this method, the organic compound is first heated with excess of HI followed by distillation of volatile iodomethane or iodoethane from the reaction mixture. Then the iodomethane or iodoethane is treated with ethanolic solution of silver nitrate, and silver iodide so formed is weighed.

5. i) Crown ethers can selectively chelate metal ions and give metal complexes, which are soluble in non polar organic solvents.
- ii) Nucleophilicity of certain anions can be enhanced by the crown ethers and hence increased the rate of reactions of such reactions.

